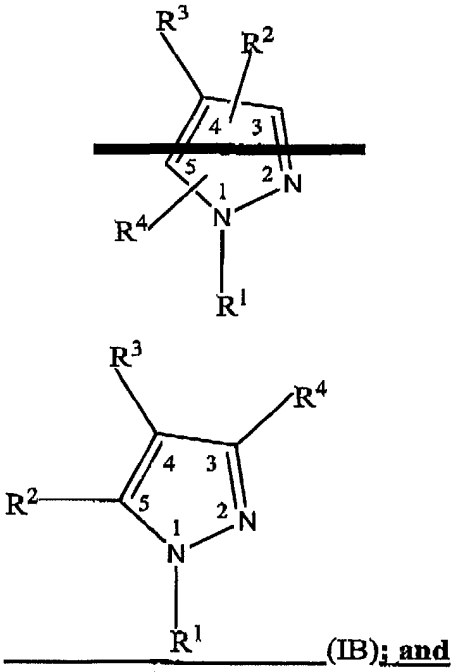
Appendix A
A Marked-Up Set of Claims Showing Amendments from Amendment C

1. **(currently amended)** A compound**, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:** ~~of~~ **the compound corresponds in structure to** Formula IB:



(IB)**; and**

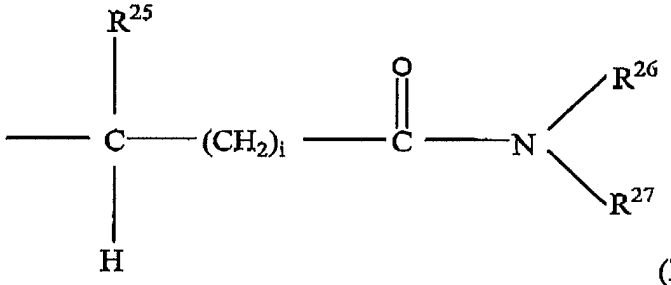
~~wherein~~

as to R^1:

R^1 is selected from **the group consisting of hydrogen** ~~hydrido~~, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, ~~aryl, heterocyclyl,~~ cycloalkylalkylene, cycloalkenylalkylene, ~~heterocyclylalkylene,~~ haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, ~~arylheterocyclyl,~~ carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, ~~heterocyclyloxyalkyl,~~ alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, ~~heterocyclylamino,~~ alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, ~~heterocyclylsulfinyl,~~ alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, ~~heterocyclylsulfonyl,~~

alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, ~~heterocyclyloxycarbonylalkylene,~~ alkoxycarbonylarylene, aryloxycarbonylarylene, ~~heterocyclyloxycarbonylarylene,~~ alkylcarbonylalkylene, arylcarbonylalkylene, ~~heterocyclylcarbonylalkylene,~~ alkylcarbonylarylene, arylcarbonylarylene, ~~heterocyclylcarbonylarylene,~~ alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, ~~heterocyclylcarbonyloxyalkylene,~~ alkylcarbonyloxyarylene, **and** arylcarbonyloxyarylene, ~~and heterocyclylcarbonyloxyarylene;~~ or

R^1 **corresponds in structure to** ~~has the~~ formula **(II):**



(II)**; and**

~~wherein:~~

i is an integer from **zero** ~~0~~ to 9; **and**

R^{25} is selected from **the group consisting of** hydrogen, alkyl, aralkyl, ~~heterocyclylalkyl,~~ alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, **and** arylcarbonylalkylene ~~, and heterocyclylcarbonylaminoalkylene~~; and

R^{26} is selected from **the group consisting of** hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxycarbonylalkylene, and alkylaminoalkyl; and

R^{27} is selected from **the group consisting of -$CHR^{28}R^{29}$,** alkyl, cycloalkyl, alkynyl, aryl, ~~heterocyclyl,~~ aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, ~~heterocyclylalkylene,~~ alkylarylene, alkylaralkyl, aralkylarylene, ~~alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl,~~ alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, ~~alkoxyheterocyclyl,~~ alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, ~~alkoxyheterocyclylalkylene,~~ aryloxyalkoxyarylene, alkoxycarbonylalkylene, ~~alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkylene,~~ aminoalkyl, alkylaminoalkylene,

arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, alkylaryloxycarbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, ~~alkoxycarbonylheterocyclylarylene,~~ alkoxycarbonylalkoxylarylene, ~~heterocyclylcarbonylalkylarylene,~~ alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene, aralkylthioarylene, ~~heterocyclylthioarylene,~~ arylthioalklylarylene, arylsulfonylaminoalkylene, alkylsulfonylarylene, **and** alkylaminosulfonylarylene~~, ;~~ wherein:

said alkyl, cycloalkyl, aryl, ~~heterocyclyl,~~ aralkyl, ~~heterocyclylalkylene, alkylheterocyclylarylene,~~ alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene, aryloxycarbonylarylene, arylcarbonylarylene, alkylthioarylene, ~~heterocyclylthioarylene,~~ arylthioalklylarylene, and alkylsulfonylarylene ~~groups~~ may be optionally substituted with one or more ~~radicals~~ **substituents** independently selected from **the group consisting of** alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano; **and** ~~or~~

~~R^{27} is $-CHR^{28}R^{29}$ wherein~~

R^{28} is alkoxycarbonyl~~; ;~~ and

R^{29} is selected from **the group consisting of** aralkyl, aralkoxyalkylene, ~~heterocyclylalkylene, alkylheterocyclylalkylene,~~ alkoxycarbonylalkylene, alkylthioalkylene, and aralkylthioalkylene~~, ;~~ wherein:

said aralkyl ~~and heterocyclyl groups~~ may be optionally substituted with one or more ~~radicals~~ **substituents** independently selected from **the group consisting of** alkyl and nitro; ~~or~~

~~R^{26} and R^{27} together with the nitrogen atom to which they are attached form a heterocycle, wherein said heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl, heterocyclyl, heterocyclylalkylene, alkylheterocyclylalkylene, aryloxyalkylene, alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl, alkoxycarbonyl, aralkoxycarbonyl, alkylamino and alkoxycarbonylamino; wherein said aryl, heterocyclylalkylene and aryloxyalkylene radicals may be optionally substituted with one or more radicals independently selected from halogen, alkyl and alkoxy;~~ and

R^2 is piperidinyl substituted with:

one or more substituents **independently** selected from **the group consisting of** hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, and hydroxyacyl, wherein:

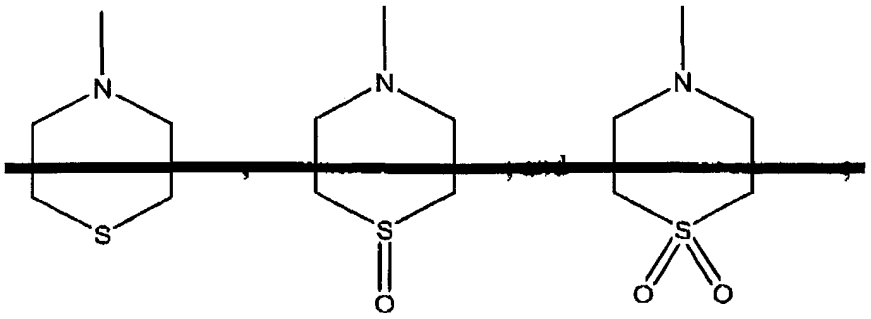
said hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, and hydroxyacyl ~~substituents~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl, ~~and heteroarylalkyl,~~ wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl ~~, and heteroarylalkyl substituents~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy, ~~heterocyclyl, and heteroaralkoxy;~~ or ~~R^2 is piperidinyl substituted with~~ one or more substituents **independently** selected from **the group consisting of** hydroxycycloalkyl and alkoxycycloalkyl, ~~and~~ wherein:

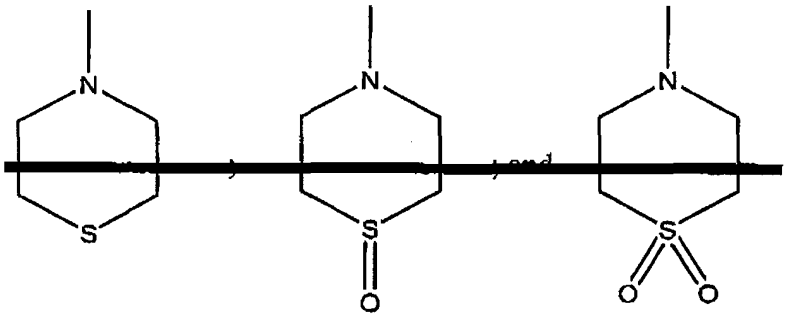
said hydroxycycloalkyl and alkoxycycloalkyl ~~substituents~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl, ~~and heteroarylalkyl,~~ wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl ~~, and heteroarylalkyl substituents~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy ~~heterocyclyl, and heteroaralkoxy~~; and

R^3 is ~~selected from~~ pyridinyl ~~, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,~~



~~wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,~~



~~groups may be~~ optionally substituted with one or more substituents independently selected from **the group consisting of** hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, **and** aralkoxy, wherein**:**

said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, **and** aralkoxy ~~substituents~~ may be optionally substituted with one or more ~~radicals~~ **substituents independently selected from the group consisting of** alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy ~~, heterocyclyl, and heteroaralkoxy~~; and

R^4 is ~~selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R^4 is~~ **phenyl** optionally substituted with one or more substituents independently selected from **the group consisting of** halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein**:**

said haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl ~~substituents~~ may be optionally substituted with one or more **substituents independently selected from the group consisting of** alkylene, alkenylene, alkynylene, hydroxy, halo,

haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy ~~**, heterocyclyl, and heteroaralkoxy; or a pharmaceutically acceptable salt or tautomer thereof**~~.

2. **(currently amended)** A compound**, tautomer, or salt** of Claim 1**,** wherein ~~**:**~~ R^2 is piperidinyl substituted with one or more substituents **independently** selected from **the group consisting of** hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl, wherein**:**

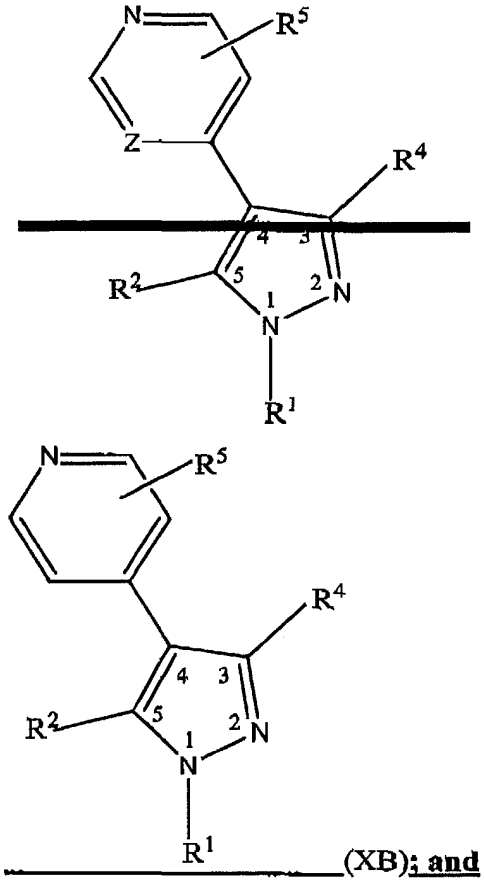
said hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl ~~**substituents**~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl, ~~**and heteroarylalkyl,**~~ wherein**:**

said cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl ~~**, and heteroarylalkyl, substituents**~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy ~~**, heterocyclyl, and heteroaralkoxy; or**~~

~~**R^2 is piperidinyl substituted with one or more substituents selected from hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl, wherein said hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl substitutents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy**~~.

Claim 3 (canceled).

4. **(currently amended)** A compound**, tautomer, or salt** of Claim 1**, wherein: ~~having~~ the compound corresponds in structure to** Formula XB:



(XB)**; and**

~~wherein~~

~~Z represents a carbon atom or a nitrogen atom;~~

R^1 is selected from **the group consisting of hydrogen ~~hydrido~~**, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, **~~aryl, heterocyclyl,~~** cycloalkylalkylene, cycloalkenylalkylene, **~~heterocyclylalkylene,~~** haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, **~~arylheterocyclyl,~~** carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, **~~heterocyclyloxyalkyl,~~** alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, **~~heterocyclylamino,~~** alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, **~~heterocyclylsulfinyl,~~** alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,

~~heterocyclylsulfonyl,~~ alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, ~~heterocyclyloxycarbonylalkylene,~~ alkoxycarbonylarylene, aryloxycarbonylarylene, ~~heterocyclyloxycarbonylarylene,~~ alkylcarbonylalkylene, arylcarbonylalkylene, ~~heterocyclylcarbonylalkylene,~~ alkylcarbonylarylene, arylcarbonylarylene, ~~heterocyclylcarbonylarylene,~~ alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, ~~heterocyclylcarbonyloxyalkylene,~~ alkylcarbonyloxyarylene, **and** arylcarbonyloxyarylene ~~, and heterocyclylcarbonyloxyarylene~~; and

R^2 is piperidinyl substituted with:

one or more substituents **independently** selected from **the group consisting of** hydroxyalkyl, hydroxyalkenyl, alkoxyalkylene, alkoxyalkenylene, hydroxyalkylcarbonyl, and hydroxyalkenylcarbonyl, wherein:

said hydroxyalkyl, hydroxyalkenyl, alkoxyalkylene, alkoxyalkenylene, hydroxyalkylcarbonyl, and hydroxyalkenylcarbonyl ~~substitutents~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl ~~, and heteroarylalkyl~~, wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl ~~, and heteroarylalkyl substituents~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy, ~~heterocyclyl, and heteroaralkoxy;~~ or ~~R^2 is piperidinyl substituted with~~ one or more substituents **independently** selected from **the group consisting of** hydroxycycloalkyl and hydroxycycloalkylcarbonyl, wherein:

said hydroxycycloalkyl and hydroxycycloalkylcarbonyl ~~substitutents~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl, ~~and heteroarylalkyl,~~ wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl ~~, and heteroarylalkyl substituents~~ may be optionally substituted with one or

more substituents **independently** selected from **the group consisting of** alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy ~~, heterocyclyl, and heteroaralkoxy~~; and

R^4 is ~~selected from cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R^4 is~~ **phenyl** optionally substituted with one or more substituents independently selected from **the group consisting of** halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein:

said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl ~~substituents~~ may be optionally substituted with one or more **substituents independently selected from the group consisting of** alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy ~~, heterocyclyl, and heteroaralkoxy~~; and

R^5 represents one or more substituents independently selected from **the group consisting of** hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, **and** aralkoxy, wherein:

said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, **and** aralkoxy ~~substituents~~ may be optionally substituted with one or more **substituents independently selected from the group consisting of** alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy ~~, heterocyclyl, and heteroaralkoxy; or a pharmaceutically-acceptable salt or tautomer thereof~~.

5. **(currently amended)** A compound**, tautomer, or salt** of Claim 4, wherein R^2 is piperidinyl substituted with at least one substituent attached to the distal nitrogen heteroatom or to a carbon ring atom adjacent to the distal nitrogen heteroatom of the piperidine ring.

Claims 6 and 7 (canceled).

8. **(currently amended)** A compound**, tautomer, or salt** of Claim 4, wherein R^1 is selected from **the group consisting of** ~~**hydrido**~~ **hydrogen**, alkyl, hydroxyalkyl, and alkynyl.

9. **(currently amended)** A compound**, tautomer, or salt** of Claim 4**,** wherein R^1 is ~~**hydrido**~~ **hydrogen**.

10. **(currently amended)** A compound**, tautomer, salt** of Claim 4**,** wherein R^2 is piperidinyl substituted with at least one substituent selected from **the group consisting of** lower hydroxyalkyl, lower hydroxyalkylcarbonyl**,** and hydroxycycloalkylcarbonyl.

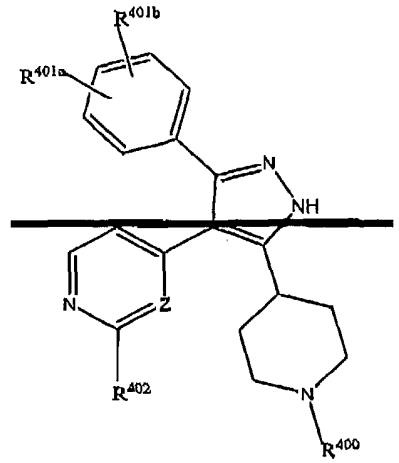
11. **(currently amended)** A compound**, tautomer, or salt** of Claim 4**,** wherein R^4 is ~~**optionally substituted**~~ phenyl **optionally substituted with one or more substituents independently selected from halo**.

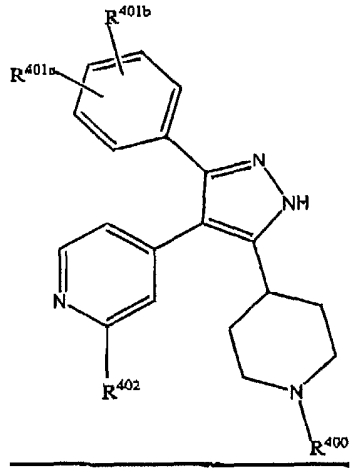
12. **(currently amended)** A compound**, tautomer, or salt** of Claim 4**,** wherein R^4 is phenyl optionally substituted ~~**at a substitutable position**~~ with one or more ~~**radicals**~~ **substituents** independently selected from **the group consisting of** chloro, fluoro, bromo**,** and iodo.

13. **(currently amended)** A compound**, tautomer, or salt** of Claim 4**,** wherein R^4 is phenyl optionally substituted at the meta or para position with one or more chloro ~~**radicals**~~ **substituents**.

14. **(currently amended)** A compound**, tautomer, or salt** of Claim 4**,** wherein R^5 is ~~**hydrido**~~ **hydrogen**.

15. **(currently amended)** A compound**, tautomer, or salt** of Claim 1**, wherein:** ~~**having**~~ **the compound corresponds in structure to** Formula XX:





(XX); **and**

~~**wherein:**~~

~~**Z represents a carbon atom or a nitrogen atom;**~~

as to R^{400}:

R^{400} is selected from **the group consisting of** hydroxyalkyl, hydroxyalkylcarbonyl, and alkoxyalkylene, wherein:

said hydroxyalkyl, hydroxyalkylcarbonyl, and alkoxyalkylene may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl, ~~**and heteroarylalkyl,**~~ wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl ~~**, and heteroarylalkyl substituents**~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of**

alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy, ~~**heterocyclyl, and heteroaralkoxy;**~~ or

R^{400} is hydroxycycloalkylcarbonyl ~~**that is**~~ optionally substituted with one or more substituents **independently** selected from **the group consisting of** cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl, ~~**and heteroarylalkyl,**~~ wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, **and** haloalkyl ~~**, and heteroarylalkyl substituents**~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy ~~**, heterocyclyl, and heteroaralkoxy**~~; and

R^{401a} and R^{401b} are independently selected from **the group consisting of** hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein:

said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl ~~**substituents**~~ may be optionally substituted with one or more **substituents independently selected from the group consisting of** alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy ~~**, heterocyclyl, and heteroaralkoxy**~~; and

R^{402} is selected from **the group consisting of** hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, **and** aralkoxy, wherein:

said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, **and** aralkoxy ~~**substituents**~~ may be optionally substituted with one or more **substituents independently selected from the group consisting of** alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, **and** aryloxy ~~**, heterocyclyl, and heteroaralkoxy; or a pharmaceutically acceptable salt or tautomer thereof**~~.

16. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein:
as to R^{400}:

R^{400} is selected from **the group consisting of** lower hydroxyalkyl, lower hydroxyalkylcarbonyl, and lower alkoxyalkylene, wherein:

said lower hydroxyalkyl, lower hydroxyalkylcarbonyl, and lower alkoxyalkylene may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, **and** lower haloalkyl, ~~**and lower heteroarylalkyl,**~~ wherein:

said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, **and** lower haloalkyl ~~**, and lower heteroarylalkyl substituents**~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** lower alkylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, **and** phenyloxy ~~**, heterocyclyl, and lower heteroaralkoxy**~~; or

R^{400} is hydroxycycloalkylcarbonyl ~~**that is**~~ optionally substituted with one or more substituents **independently** selected from **the group consisting of** cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, **and** lower haloalkyl, ~~**and lower heteroarylalkyl,**~~ wherein:

said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, **and** lower haloalkyl ~~**, and lower heteroarylalkyl substituents**~~ may be optionally substituted with one or more substituents **independently** selected from **the group consisting of** lower alkylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, **and** aryloxy ~~**, heterocyclyl, and lower heteroaralkoxy**~~; and

R^{401a} and R^{401b} are independently selected from **the group consisting of** hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein:

said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl ~~**substituents**~~ may be optionally substituted with one or more **substituents independently selected from the group consisting of** lower

alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, **and** phenyloxy ~~, heterocyclyl, and lower heteroaralkoxy~~; and

R^{402} is selected from **the group consisting of** hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein:

said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or more **substituents independently selected from the group consisting of** lower alkylene, lower alkenylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, **and** phenyloxy ~~, heterocyclyl, and lower heteroaralkoxy; or a pharmaceutically acceptable salt or tautomer thereof~~.

Claims 17 and 18 (canceled).

19. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein R^{400} is optionally substituted hydroxyalkylcarbonyl.

20. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein R^{400} is optionally substituted hydroxycycloalkylcarbonyl.

21. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein R^{400} is optionally substituted alkoxyalkylene.

22. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein R^{400} is optionally substituted hydroxyalkyl.

23. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein ~~R^{401}~~ **R^{401a}** ~~represents one or more~~ **is selected from the group consisting of** chloro, fluoro, bromo, and iodo.

24. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein ~~R^{401}~~ **R^{401a}** is **selected from the group consisting of** meta-chloro ~~or~~ **and** para-chloro.

25. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein R^{402} is ~~hydrido~~ **hydrogen**.

26. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein:
R^{400} is optionally substituted lower hydroxyalkylcarbonyl; **and**
R^{401a} is selected from **the group consisting of** chloro, fluoro, bromo, and iodo; and
R^{402} is ~~hydrido~~ **hydrogen**.

27. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein:
R^{400} is selected from **the group consisting of** optionally substituted 2-hydroxyacetyl, 2-hydroxy-proprionyl, 2-hydroxy-2-methylpropionyl, 2-hydroxy-2-phenylacetyl, 3-hydroxyproprionyl, 2-hydroxy-3-methylbutyryl, 2-hydroxyisocapropyl, **and** 2-hydroxy-3-phenylproprionyl ~~, and 2-hydroxy-3-imidazolylproprionyl~~; **and**
R^{401a} is selected from **the group consisting of** chloro, fluoro, bromo, and iodo; and
R^{402} is ~~hydrido~~ **hydrogen**.

28. **(currently amended)** A compound, **tautomer, or salt** of Claim 27, wherein R^{401a} is **selected from the group consisting of** meta-chloro ~~or~~ **and** para-chloro.

29. **(currently amended)** A compound, **tautomer, or salt** of Claim 27, wherein:
R^{401a} is para-chloro, and
R^{401b} is hydrogen.

30. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein:
R^{400} is optionally substituted lower hydroxycycloalkylcarbonyl; **and**
R^{401a} is selected from **the group consisting of** chloro, fluoro, bromo, and iodo; and
R^{402} is ~~hydrido~~ **hydrogen**.

31. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein:

R^{400} is selected from **the group consisting of** optionally substituted 1-hydroxy-1-cyclohexylacetyl, 2-hydroxy-1-cyclohexylacetyl, 3-hydroxy-1-cyclohexylacetyl, 4-hydroxy-1-cyclohexylacetyl, 1-hydroxy-1-cyclopentylacetyl, 2-hydroxy-1-cyclopentylacetyl, and 3-hydroxy-1-cyclopentylacetyl, 2-hydroxy-2-cyclohexylacetyl; **and**

R^{401a} is selected from **the group consisting of** chloro, fluoro, bromo, and iodo; and

R^{402} is ~~**hydrido**~~ **hydrogen**.

32. **(currently amended)** A compound, **tautomer, or salt** of Claim 31, wherein R^{401a} is **selected from the group consisting of** meta-chloro ~~**or**~~ **and** para-chloro.

33. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein:

R^{400} is optionally substituted lower hydroxyalkyl; **and**

R^{401} is selected from **the group consisting of** chloro, fluoro, bromo, and iodo; and

R^{402} is ~~**hydrido**~~ **hydrogen**.

34. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein:

R^{400} is selected from **the group consisting of** optionally substituted hydroxymethyl, hydroxyethyl, hydroxypropyl and hydroxyisopropyl; **and**

R^{401a} is selected from **the group consisting of** chloro, fluoro, bromo, and iodo; and

R^{402} is ~~**hydrido**~~ **hydrogen**.

35. **(currently amended)** A compound, **tautomer, or salt** of Claim 34, wherein R^{401a} is **selected from the group consisting of** meta-chloro ~~**or**~~ **and** para-chloro.

36. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein:

R^{400} is optionally substituted lower alkoxyalkylene; **and**

R^{401a} is selected from **the group consisting of** chloro, fluoro, bromo, and iodo; and

R^{402} is ~~**hydrido**~~ **hydrogen**.

37. **(currently amended)** A compound, **tautomer, or salt** of Claim 15, wherein:

R^{400} is selected from **the group consisting of** optionally substituted methoxymethylene, methoxyethylene, methoxypropylene, methoxyisopropylene, ethoxymethylene, ethoxyethylene, ethoxypropylene, and ethoxyisopropylene**; and** ;

R^{401a} is selected from **the group consisting of** chloro, fluoro, bromo, and iodo; and

R^{402} is ~~**hydrido**~~ **hydrogen**.

38. **(currently amended)** A compound, **tautomer, or salt** of Claim 37, wherein R^{401a} is **selected from the group consisting of** meta-chloro ~~**or**~~ **and** para-chloro.

Claims 39-131 (canceled).

132. **(currently amended)** A pharmaceutical composition, **wherein:**

the pharmaceutical composition comprises ~~**comprising**~~ a therapeutically-effective amount of a compound **or a pharmaceutically-acceptable salt of the compound; and** ;

said compound **is** selected from the **group consisting of** compounds **recited in claim** ~~**of any one of Claims**~~ 1 ~~**, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof**~~.

133. **(currently amended)** A method **for** ~~**of**~~ treating a ~~**TNF**~~ **tumor necrosis factor** mediated disorder, **wherein:**

said method **comprises** ~~**comprising**~~ treating **a** ~~**the**~~ subject having or susceptible to such disorder with a therapeutically-effective amount of a compound **or a pharmaceutically-acceptable salt thereof, and**

said compound **is** selected from the **group of** compounds **recited in claim** ~~**of any one of Claims**~~ 1 ~~**, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof**~~.

134. **(currently amended)** A method **for** ~~**of**~~ treating a p38 kinase mediated disorder, **wherein:**

said method **comprises** ~~**comprising**~~ treating **a** ~~**the**~~ subject having or susceptible to such disorder with a therapeutically-effective amount of a compound **or a pharmaceutically-acceptable salt thereof, and**

said compound **is** selected from the **group of** compounds **recited in claim** ~~**of any one of Claims**~~ 1 ~~**, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof**~~.

135. **(original)** The method of Claim 134 wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis, inflammatory bowel disease and cachexia.

136. **(original)** The method of Claim 134 wherein the p38 kinase mediated disorder is inflammation.

137. **(original)** The method of Claim 134 wherein the p38 kinase mediated disorder is arthritis.

138. **(original)** The method of Claim 134 wherein the p38 kinase mediated disorder is asthma.

139. **(currently amended)** A method **for** ~~**of**~~ treating inflammation, **wherein:**

said method **comprises** ~~**comprising**~~ treating **a** ~~**the**~~ subject having or susceptible to inflammation with a therapeutically-effective amount of a compound **or a pharmaceutically-acceptable salt thereof, and**

said compound **is** selected from the **group of** compounds **recited in claim** ~~**of any one of Claims**~~ 1 ~~**, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof**~~.

140. **(currently amended)** A method **for** ~~**of**~~ treating arthritis, **wherein:**

said method **comprises** ~~**comprising**~~ treating **a** ~~**the**~~ subject having or susceptible to arthritis with a therapeutically-effective amount of a compound **or a pharmaceutically-acceptable salt thereof, and**

said compound **is** selected from the **group of** compounds **recited in claim** ~~**of any one of Claims** 1 **, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof**~~.

Claims 141-160 (canceled).

161. **(new)** A pharmaceutical composition, wherein:

the pharmaceutical composition comprises a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt of the compound; and

said compound is selected from the group consisting of compounds recited in claim 4.

162. **(new)** A method for treating a tumor necrosis factor mediated disorder, wherein:

said method comprises treating a subject having or susceptible to such disorder with a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt thereof, and

said compound is selected from the group of compounds recited in claim 4.

163. **(new)** A method for treating a p38 kinase mediated disorder, wherein:

said method comprises treating a subject having or susceptible to such disorder with a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt thereof, and

said compound is selected from the group of compounds recited in claim 4.

164. **(new)** The method of Claim 163, wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis, inflammatory bowel disease, and cachexia.

165. **(new)** The method of Claim 163, wherein the p38 kinase mediated disorder is inflammation.

166. **(new)** The method of Claim 163, wherein the p38 kinase mediated disorder is arthritis.

167. **(new)** The method of Claim 163, wherein the p38 kinase mediated disorder is asthma.

168. **(new)** A method for treating inflammation, wherein:

said method comprises treating a subject having or susceptible to inflammation with a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt thereof, and

said compound is selected from the group of compounds recited in claim 4.

169. **(new)** A method for treating arthritis, wherein:

said method comprises treating a subject having or susceptible to arthritis with a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt thereof, and

said compound is selected from the group of compounds recited in claim 4.

170. **(new)** A pharmaceutical composition, wherein:

the pharmaceutical composition comprises a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt of the compound; and

said compound is selected from the group consisting of compounds recited in claim 15.

171. **(new)** A method for treating a tumor necrosis factor mediated disorder, wherein:

said method comprises treating a subject having or susceptible to such disorder with a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt thereof, and

said compound is selected from the group of compounds recited in claim 15.

172. **(new)** A method for treating a p38 kinase mediated disorder, wherein:

said method comprises treating a subject having or susceptible to such disorder with a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt thereof, and

said compound is selected from the group of compounds recited in claim 15.

173. **(new)** The method of Claim 172, wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis, inflammatory bowel disease, and cachexia.

174. **(new)** The method of Claim 172, wherein the p38 kinase mediated disorder is inflammation.

175. **(new)** The method of Claim 172, wherein the p38 kinase mediated disorder is arthritis.

176. **(new)** The method of Claim 172, wherein the p38 kinase mediated disorder is asthma.

177. **(new)** A method for treating inflammation, wherein:

said method comprises treating a subject having or susceptible to inflammation with a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt thereof, and

said compound is selected from the group of compounds recited in claim 15.

178. **(new)** A method for treating arthritis, wherein:

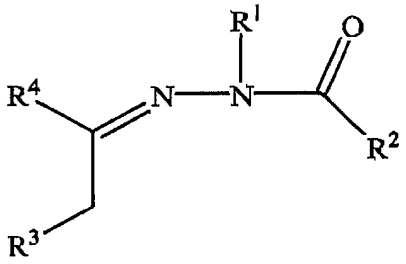
said method comprises treating a subject having or susceptible to arthritis with a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt thereof, and

said compound is selected from the group of compounds recited in claim 15.

179. **(new)** A process for making a compound, tautomer, or salt recited in claim 1, wherein:

the process comprises cyclizing an acyl hydrazone to form a compound corresponding in structure to Formula IB; and

the acyl hydrazone corresponds in structure to the following formula:



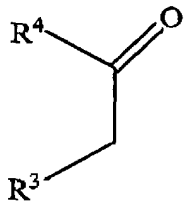
; and

Formula IB, R^1, R^2, R^3, and R^4 are as defined in claim 1.

180. **(new)** The process according to Claim 179, wherein:

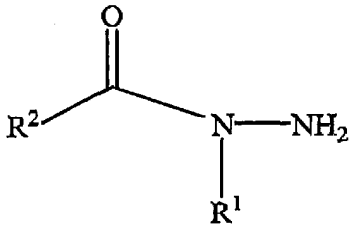
the acyl hydrazone is formed by a process comprising reacting a ketone with an acyl hydrazide; and

the ketone corresponds in structure to the following formula:



; and

the acyl hydrazide corresponds in structure to the following formula:



; and

R^1, R^2, R^3 and R^4 are as defined in Claim 179.

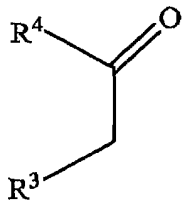
180. **(new)** The process according to Claim 179, wherein:

the acyl hydrazone is formed by a process comprising:

reacting a ketone with a hydrazine to form a substituted hydrazide, and

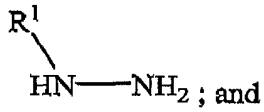
reacting the substituted hydrazide with an acyl halide; and

the ketone corresponds in structure to the following formula:



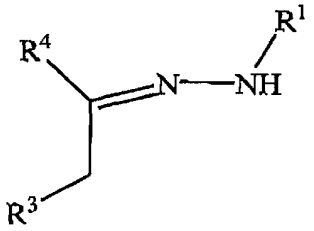
; and

the hydrazine corresponds in structure to the following formula:



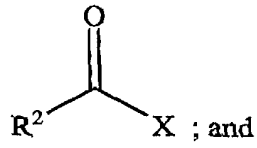
; and

the substituted hydrazide corresponds in structure to the following formula:



; and

the acyl halide corresponds in structure to the following formula:



; and

X is halogen; and

R^1, R^2, R^3 and R^4 are as defined in Claim 179.